

## Next Generation Strategies for Gene-Targeted Therapies of Central Nervous System Disorders

**September 26-27, 2019**

*Bethesda North Marriott*

Co-Chairs:

Beverly Davidson, Ph.D. & Guangping Gao, M.D., Ph.D.

**Objective:** Recent advances in the gene therapy field have contributed to renewed interest in gene replacement, gene silencing, and genome editing as approaches to gene-targeted therapeutic strategies. This workshop will bring together a multi-disciplinary group of experts from academia, government, and industry to identify key challenges/gaps and opportunities, and to provide insight on how NIH could facilitate these next generation strategies for patients with neurological or neuromuscular disorders.

### AGENDA

#### Thursday, September 26

8:00 – 8:30 AM	<b>Registration</b>
8:30 – 8:40 AM	<b>Welcome &amp; Opening Remarks</b> – <i>Nina Schor, NINDS Deputy Director</i>
8:40 – 8:50 AM	<b>Meeting Expectations</b> – <i>Jill Morris &amp; Chris Boshoff, NINDS Program Directors</i>
8:50 – 9:10 AM	<b>A Summary of Key Challenges for the Field</b> – <i>Beverly Davidson, Co-Chair</i>
9:10 – 9:30 AM	<b>Teamwork Approaches to Address the Challenges in CNS Therapy by rAAV</b> – <i>Guangping Gao, Co-Chair</i>
	<b>Session I: Control of Level &amp; Location</b> Session Chairs: <i>Beverly Davidson &amp; Steven Gray</i>
9:30 – 9:45 AM	<b>Overview</b>
9:45 – 10:30 AM	<b>Session 1A: Regulated Expression</b> <ul style="list-style-type: none"> <li>• Avoiding overexpression</li> <li>• Knockdown/inhibition; gene silencing</li> <li>• Unique challenges with cell autonomous gene therapy</li> </ul>
10:30 – 10:45 AM	<b>Break</b>
10:45 – 11:30 AM	<b>Session 1B: Focused Targeting</b> <ul style="list-style-type: none"> <li>• Enhancing specificity to specific cells or tissues</li> <li>• Detecting &amp; minimizing off-target effects</li> </ul>
11:30 – 11:45 AM	<b>Open Discussion</b>

11:45 – 12:45 PM	<b>Lunch</b> ( <i>on your own</i> )
<b>Session 2: Improving Delivery &amp; Distribution</b> Session Chairs: <i>Guangping Gao &amp; Viviana Gradinaru</i>	
12:45 – 1:00 PM	<b>Overview</b>
1:00 – 1:45 PM	<b>Session 2A: The Present</b> <ul style="list-style-type: none"> <li>• CNS-specific immune responses for different routes</li> <li>• Validating vector distribution</li> <li>• Does immunosuppression help?</li> </ul>
1:45 – 2:30 PM	<b>Session 2B: The Future</b> <ul style="list-style-type: none"> <li>• Translation of novel delivery methods</li> <li>• Strategies to develop better AAV vectors, or non-AAV vector systems</li> <li>• Enabling second administration</li> </ul>
2:30 – 2:45 PM	<b>Open Discussion</b>
2:45 – 3:00 PM	<b>Break</b>
<b>Session 3: Enhancing Models &amp; Manufacturing</b> Session Chairs: <i>Heather Gray &amp; Fraser Wright</i>	
3:00 – 3:15 PM	<b>Overview</b>
3:15 – 4:00 PM	<b>Session 3A: Preclinical Models</b> <ul style="list-style-type: none"> <li>• Predictive validity of treatment response</li> <li>• Ideal models of immune response</li> <li>• Assessing &amp; translating long-term effects</li> <li>• Feasibility of standardizing assays</li> </ul>
4:00 – 4:45 PM	<b>Session 3B: Manufacturing</b> <ul style="list-style-type: none"> <li>• Manufacturing challenges</li> <li>• Impact of batch vector production on ultra-rare diseases</li> <li>• Feasibility of standardizing procedures</li> </ul>
4:45 – 5:00 PM	<b>Open Discussion</b>

## Friday, September 27

8:00 – 8:30 AM	<b>Registration</b>
8:30 – 8:40 AM	<b>Opening Remarks</b> – <i>Walter Koroshetz, NINDS Director</i>
	<b>Session 4: Impacting Patients</b> Session Chairs: <i>Carsten Bönnemann &amp; Krystof Bankiewicz</i>
8:40 – 9:45 AM	<b>Setting the Stage</b> <u>Gene Therapy Clinical Trials</u> Carsten Bonnemann, M.D. Senior Investigator, Neuromuscular and Neurogenetic Disorders of Childhood Section, NINDS  Krystof Bankiewicz, M.D., Ph.D. Professor, Department of Neurological Surgery, The Ohio State University  <u>NIH Collaboration Models</u> Stephanie Morris, Ph.D. Program Officer, Office of Strategic Coordination, NIH  <u>Network exemplar: Children's Oncology Group</u> Nita Seibel, M.D Medical Officer, NCI
9:45 – 9:55 AM	<b>Break</b>
9:55 – 10:00 AM	<b>Overview</b>
10:00 – 10:40 AM	<b>Session 4A: Clinical Trials &amp; FDA Regulation</b> <ul style="list-style-type: none"> <li>• Clinical trial readiness</li> <li>• Key issues in implementing innovative/adaptive trial design</li> <li>• Feasibility of standardizing clinical procedures/measurements</li> <li>• Streamlined regulatory processes</li> </ul>
10:40 – 11:20 AM	<b>Session 4B: Clinical Networks</b> <ul style="list-style-type: none"> <li>• Leveraging the NIH Clinical Center</li> <li>• Is a Consortium needed? What could it do, and how?</li> </ul>
11:20 – 11:30 AM	<b>Break</b>
	<b>Session 5: Bringing it All Together</b> Session Chairs: <i>Jill Morris &amp; Chris Boshoff</i>
11:30 – 12:10 PM	<b>Summary Recommendations</b> – <i>Session 1-4 Chairs</i>
12:10 – 12:40 PM	<b>Strategy Development</b> – <i>Open Discussion</i> <ul style="list-style-type: none"> <li>• What could the research field, NINDS, and/or NIH do?</li> <li>• What are the gaps (in knowledge, infrastructure, etc)?</li> <li>• Which roadblocks are immediately/feasibly addressable?</li> <li>• What are realistic goals? Which are highest priority?</li> <li>• What is an appropriate timeline?</li> </ul>
12:40 – 12:45 PM	<b>Closing remarks</b> – <i>Jill Morris &amp; Chris Boshoff</i>
12:45 PM	<b>Adjourn</b>